MEETING MINUTES
OF THE

CLINICAL CHEMISTRY
AND
CLINICAL TOXICOLOGY DEVICES PANEL

OF THE
MEDICAL DEVICES ADVISORY COMMITTEE

September 25, 1997

OPEN SESSION

Holiday Inn - Bethesda
8120 Wisconsin Avenue
Bethesda, MD

Clinical Chemistry and Clinical Toxicology Devices Panel Meeting

September 25, 1997

Attendees

Henry Nipper, Ph.D.
Chairperson

Sharon Lappalainen, M.T. (ASCP)
Executive Secretary

Voting Members
Joann Boughman, Ph.D.
Barbara Goldsmith, Ph.D.
Robert Rej, Ph.D.
Thomas Kurt, M.D.
Beverly Harrington Falls, M.D.

Consultants
David Sohn, M.D.
Barbara R. Manno, Ph.D.
Benjamin Gerson, M.D.
James Everett, M.D., Ph.D.
Theodore Tong, Pharm.D.
Sherwood C. Lewis, Ph.D.

Industry Representative
Robert Habig, Ph.D.

Consumer Representative
Ellen S. Rosenthal, M.S.

FDA Representatives
Alfred W. Montgomery, D.V.M.
Steven I. Gutman, M.D., M.B.A.
Patricia A. Kingsley, B.S.N., M.G.A.

SAMHSA Official Liaison
Donna M. Bush, Ph.D.

The Clinical Chemistry and Clinical Toxicology Devices Advisory Panel met on September 25, 1997, to discuss a draft guidance document entitled "Points To Consider For Approval of Home Drugs of Abuse Tests." The meeting began with an update regarding the subject of the panel meeting of March 20 & 21, 1997. The panel was told of the recent clearance to market for an over-the-counter (OTC) device that measures fructosamine and of the FDA's efforts to provide a revised version of the guidance document entitled "Review Criteria for the Assessment of Portable Blood Glucose Monitoring In Vitro Diagnostic Devices Using Glucose Oxidase, Dehydrogenase, or Hexokinase Methodology."

Open Public Session. Panelists heard presentations from a number of manufacturers of drugs of abuse tests, private individuals, and the laboratory testing community. Most speakers thought that use of illegal drugs by youth had reached epidemic proportions in the United States. Some maintained that home drug testing kits would be helpful to parents because they could be used as a prevention tool, as a deterrent to peer pressure, and as catalysts for communication. Other speakers stressed the importance of parent's access to tests and the privacy, convenience, and confidential nature afforded by home testing.

Some speakers asserted that lay users needed more guidance than just package labeling for interpretation of home use drug tests, that results from screening tests should have a high level of accuracy, that results be confirmed with a more accurate confirmation method, that educational material be provided with the test kits, and that professional counseling be provided to aid in the interpretation of drug screening tests.

However, some speakers maintained that interpretation of existing drug screening tests is often problematic because of sample cross-reactive substances or adulterants from many OTC drugs, and of delays in obtaining a laboratory confirmation test. Still others questioned whether home drug tests could provide results that were as accurate as those provided by the gas chromatography/mass spectrometry (GC/MS) confirmatory method, could home tests differentiate between available OTC medications and illicit drugs use, and would parents seek laboratory confirmation of a result? A few speakers felt that existing rapid screening technologies were not accurate enough for home use and that laboratory testing with confirmation and professional intervention was the best approach. Most speakers thought that the rapid tests were accurate enough if used in combination with a laboratory confirmation and with counseling services, and that appropriate labeling could overcome technical difficulties associated with drug screening tests.

FDA Presentation. FDA's presentation stated the meeting objectives and reviewed the regulatory history of OTC drugs of abuse tests. The speaker described the development of new regulatory approaches that revisited current science, outlined the use and labeling of these products, and of efforts to work with manufacturers and the professional community in a search for mechanisms that allow for the marketing of home drugs of abuse tests in a safe and effective manner. The panel was asked to address six questions: (1) Are the performance recommendations outlined in the draft points to consider adequate to characterize these tests? Should any additional data sets be requested? (2) What studies are appropriate to ensure that

these tests produce acceptable performance in the hands of home users? (3) What recommendations can you make about appropriate labeling for these devices for use by lay users? In particular, what mechanisms should be used to communicate test performance limitations to users? (4) What performance standards are appropriate to establish safety and effectiveness of these devices? (5) What considerations should FDA use to encourage/communicate the need for confirmatory testing and for dealing with other recommendations commonly associated with the NIDA/SAMHSA regulatory paradigm? (6) How should FDA address the issue of quality control of these products in the home environment?

SAMHSA Presentation. A SAMHSA spokesperson described the Federal Drug-Free Workplace Program that was developed to support the drug testing element of a comprehensive drug-free workplace program. The speaker described the National Laboratory Certification Program that certifies drug testing laboratories and the two-tiered testing system approach: an initial test followed by a confirmatory test, if the initial test was presumptive positive. The two-tiered approach was instituted to ensure accurate and reliable results, to protect the interests of the Federal Government and those drug tested under Federal authority. The spokesperson then discussed some data obtained from certified laboratories that indicated that substances cross-react with the initial screening tests that were used and that this immunoassay screen, when used in the laboratory setting, determines those specimens which go on to confirmation. The spokesperson asserted that immunoassay screens do not determine unequivocally which specimens are drug

positive and that there is a failure to confirm rate associated with these tests. Data from another study that evaluated non-instrumented drug test devices was also discussed. The authors of the study evaluated ease-of-use, ability to interpret a result, and other factors. The study found that some devices required multiple steps resulting in operator variability, and that reading the test result was often difficult or interpreted as equivocal. When the results of the non-instrumented drug test devices were confirmed by GC/MS, there were a number of specimens that failed to test positive, when they contained confirmable quantities of drug. The SAMHSA speaker concluded that these data prompt many questions concerning home drug testing kits and the acceptability of results using immunoassays alone, the risks and benefits associated with home drug tests, and that most kits do not measure some commonly abused drugs such as alcohol, LSD, and inhalants.

FDA Presentation. FDA outlined the challenges involved in developing product labeling for home use medical devices. The challenges that were discussed included reading level or readability and the issue of limiting the material that should be presented in the labeling balanced by the need for comprehensiveness. Other challenges that were pointed out, were the use/over-use of highlighting, overcoming transference of knowledge, and problem anticipation. The speaker described some tools that are available that deal with the basic challenge of OTC labeling, but that do not specifically target the unique challenges that were previously discussed, such as the use of color, pictures, symbols that are targeted to focus attention on labeling instructions.

Open Committee Discussion. Panelists asked a number of questions and requested clarification concerning the data sets that were discussed by the SAMHSA spokesperson. Issues that were questioned included how the workplace screening cutoffs were determined versus how should the home use cutoffs be determined, what would constitute appropriate performance parameters for home tests, and how should these parameters be determined.

Regarding the six questions that the panelists were asked to address, on the first question, panelists agreed that performance testing needs to be comprehensive, be conducted on the population for which the test is intended, and be appropriate to the intended user of the test. Panelists questioned whether confirmation of just positive results would be sufficient, and whether negative results should be confirmed as well. Several panelists stressed the importance of samples being assessed for possible adulteration, e.g., by dilution, use of contaminants, temperature strips, etc. The panelists also recommended that false positive and false negative rates of home tests be determined using GC/MS.

On the second question, panelists recommended that the accuracy of home test kits for drugs of abuse be evaluated in the home environment, that demographic information be obtained from the population to be tested, and that a consumer survey be developed. Panelists also suggested that test sensitivity, specificity, positive predictive value, negative predictive value, and efficiency be addressed by manufacturers of these test kits. In addition, the panel indicated that it would be important to question what would be an acceptable medical allowable error and a tolerable error rate associated with home drugs of abuse tests.

On the third question, the panel had a number of labeling recommendations and

mechanisms for communicating test performance limitations. Panelists agreed that simplicity is paramount. Labeling suggestions included: the use of pictures whenever possible, simple to read instructions, the inclusion of a 1-800 or resource number for professional advice, and that confirmation of test results be included. Panelists also recommended that the package insert be directed towards an appropriate level of reading comprehension, that instructions should be simple, and should clearly indicate what substances are being tested.

Regarding the fourth question, panelists were unsure as to what performance standards should be imposed; however, they agreed that it would be important not to relax existing performance standards for home tests over those standards required by the laboratory.

On the fifth question, panelist felt that sponsors should clearly state whether the test was intended for screening or for diagnostic use. The panelists agreed that confirmation by GC/MS of all presumptive positive results should be required and included as part of the home use test.

Regarding the sixth question, panelists suggested that quality control mechanisms be included or built-in to the test design, that the quality control mechanism be specific to the test principle and not simply be a process control, and that tests for sample adulteration be included.

ADJOURNMENT

The meeting was adjourned at 4:37 p.m.

I certify that I attended the meeting of the Clinical Chemistry and Clinical Toxicology Devices Panel on September 25, 1997, and that these minutes accurately reflect what transpired.

Sharon Lappalainen, M.T. (ASCP)
Executive Secretary, FDA

I approve the minutes of this meeting as recorded in this summary.

Henry C. Nipper, Ph.D.
Chairperson